UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,561	03/19/2002	Jerry M Collins	31978-178825	6698

26694 7590 02/24/2004

VENABLE, BAETJER, HOWARD AND CIVILETTI, LLP
P.O. BOX 34385
WASHINGTON, DC 20043-9998

EXAMINER	
JONES, DAMERON LEVEST	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 02/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,561	COLLINS ET AL.	
	Examiner	Art Unit	
	D. L. Jones	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31 and 41-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *20-39* is/are allowed.

6)☒ Claim(s) *1-19, 41, and 43-49* is/are rejected.

7)☒ Claim(s) *42* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

ACKNOWLEDGMENTS

1. The Examiner acknowledges receipt of the amendment filed 11/21/03 wherein the specification was amended; claims 3, 7, 12, and 19 were amended; claims 32-40 were canceled; and claims 41-49 were added.

Note: Claims 1-31 and 41-49 are pending.

RESPONSE TO RESTRICTION COMMENTS

2. The Examiner has read Applicant's response to the restriction requirement. Specifically, Applicant has amended some of the dependent claims to encompass taxanes as a genus. Applicant has requested that claims 25-27, 30, and 31 be examined with the other claims directed to taxanes. Applicant has also stated that should the claims (25-27, 30, and 31) be examined with the other claims, claim 1 will be amended to refer to taxanes only.

The Examiner acknowledges Applicant's request and will examine the genus taxane; however, *all independent claims* (1, 8, 13, and 41) should be amended to include taxanes only, not just independent claim 1. Thus, all pending claims are being examined as if they read on taxanes only.

RESPONSE TO APPLICANT'S ARGUMENTS/AMENDMENT

3. The Applicant's arguments filed 11/21/03 to the rejection of claims 1-24 made by the Examiner under 35 USC 103 have been fully considered and deemed persuasive. Therefore, the said rejection is hereby withdrawn.

Note #1: The rejection has been withdrawn because the primary reference specifically discloses that paclitaxel is excluded from their invention (column 3, lines 17-40, note that R and R' cannot both be hydrogen which would result in the compound paclitaxel).

Note #2: It should be noted that even though the 103(a) rejection over Page et al (US Patent No. 5,981,564) in view of Li et al (US Patent No. 6,441,0225) in further view of Schirbel (Berichhte des Forschungszentrums Julich (1998), 3602, pp. 1-110), has been withdrawn as it relates to paclitaxel, since the claims read on the genus taxanes, and glutaryl paclitaxel compounds are encompassed within the taxane genus, the claims are still rejectable under 103(a) as set forth below.

NEW GROUNDS OF REJECTION

112 Rejections

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 43-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims as written are ambiguous because it appears as if Applicant intended the claims to read upon claim 42 instead of claim 41.

103 Rejections

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-19 and 41-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Page et al (US Patent No. 5,981,564) in view of Li et al (US Patent No. 6,441,0225) in further view of Schirbel (Berichhte des Forschungszentrums Julich (1998), 3602, pp. 1-110).

Page et al disclose paclitaxel derivatives having an increased solubility in water (see entire document, especially, abstract). The derivatives may be used to detect apoptosis of cells, for in vivo treatment or prophylaxis of cancer by administering a therapeutically effective amount of the derivative to a patient in need, or for in vivo labeling of tubulin (column 2, lines 44-68). Page discloses that the paclitaxel derivative may be labeled with a marker such as a fluorescent marker or a radioactive marker (column 3, lines 1-13 and 48-51). The water-soluble paclitaxel derivatives have Formula I as set forth in column 3, lines 17-40. However, Page et al fail to (a) disclose specifically disclose carbon-11 labeled compounds even though the document discloses that paclitaxel derivatives may be labeled; (b) specifically state that the paclitaxel derivatives may be imaged by positron emission tomography; (c) disclose that 11C-paclitaxel may be used in combination with other drugs or with modulators; and (d)

disclose all the possible types of cancers/tumors that may be treated with paclitaxel derivatives.

Li et al disclose water-soluble compositions of paclitaxel formed by conjugating the paclitaxel to a water-soluble polymer such as polyglutamic acid, polyaspartic acid, or polylysine. The compositions are useful for the treatment of tumors (see entire document, especially, abstract). In addition, Li et al disclose that their compositions provide water soluble taxoids that overcome the drawbacks associated with the insolubility of the drugs themselves and provide the advantages of improved efficacy and controlled release so that tumors may be eradicated after a single intravenous administration (column 3, lines 22-28). The methods of Li et al may be used to make water-soluble polymer conjugates of other therapeutic agents, contrast agents, and drugs. The conjugates may be administered in conjunction with other drugs including anti-tumor/anti-cancer drugs. The water-soluble paclitaxel compositions may, in certain types of treatment, be combined with a platinum drug, an anti-tumor agent (e.g., doxorubicin or daunorubicin), other drugs, or combined with external or internal irradiation (column 3, lines 49-59). The compositions of Li et al may contain a radionuclide and be used as an anti-tumor agent or drug. The pharmaceutical composition may include a therapeutic amount of a chelated radioactive isotope (column 6, lines 14-18). The paclitaxel compositions may be used to treat cancer by administering a pharmaceutically acceptable composition to a subject in an amount effective to treat the tumor. The compositions of Li et al are effective against any type of cancer including breast cancer, ovarian cancer, malignant melanoma, lung cancer,

head cancer, and neck cancer. Also, Li et al disclose that the use of the term 'treating' cancer as set forth in their invention is understood as meaning any medical management of a subject having a tumor (column 6, lines 46-65). Radiolabeled paclitaxel compositions are useful in imaging tumors. One is able to determine whether paclitaxel compositions will be taken up by a particular tumor by imaging techniques such as positron emission tomography or single photon emission computer tomography. This determination may then be used to predict the efficacy of an anti-cancer treatment (column 14, lines 19-30).

Schirbel discloses that carbon-11 is a positron emission tomography radioindicator that offers unique possibility of authentic labeling of molecules for non-invasive and quantitative determination of physiological functions (see entire document, especially, page 1, 'Synthesis of n.c.a. PET-radiotracers with carbon-11).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Page et al using the teachings of Schirbel and Li et al and generate compounds and methods of use thereof comprising 11C-taxane complexes for the reasons set forth below. (1) Page et al disclose paclitaxel derivatives (glutaryl paclitaxel compounds) which are encompassed within the taxane genus may be radiolabeled. (2) Li et al discloses paclitaxel conjugates that may also be radiolabeled and used for various imaging techniques including positron emission tomography. (3) Schirbel discloses that carbon-11 offers unique possibilities of authentic labeling of molecules as radioindicators for non-invasive and quantitative determination of physiological functions via positron emission tomography. (4) Li et al

disclose that paclitaxel conjugates are effective against any type of cancer/tumor including breast cancer, ovarian cancer, malignant melanoma, lung cancer, head and neck cancer, gastric cancer, prostate cancer, colon cancer, leukemia, and Kaposi's Sarcoma (column 6, lines 46-57). (5) Also, it should be noted that Li et al disclose that 'modulators', water soluble polymers, may be conjugated to paclitaxel complexes to overcome the drawbacks associated with the insolubility of the drugs themselves and to provide the advantages of improved efficacy and controlled release so that tumors may be eradicated after a single administration of the drug (column 3, lines 22-28). (6) Furthermore, Li et al disclose that it is known in the art to use anti-tumor/anti-cancer drugs in combination. For example, paclitaxel conjugates may be used in combination with other drugs such as doxorubicin or combined with external or internal irradiation (column 3, lines 49-59).

Since each of the references cited disclose paclitaxel derivatives that are encompassed with the taxane genus, the documents may be considered to be within the same field of endeavor. Hence, the references are combinable.

ALLOWABLE CLAIMS

8. Claims 20-39 are allowable over the prior art of record because the prior art neither anticipates nor renders obvious compounds (and uses thereof) as set forth in independent claim 20 containing at least one carbon-11.

CLAIM OBJECTION

9. Claim 42 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Note: Claim 42 is allowable over the prior art of record because the prior art neither anticipates nor renders obvious compounds as set forth in claim 42 for measuring the accumulation of antitumor drugs by solid tumors having the limitation of independent claim 41.

COMMENTS/NOTES

10. In claim 20, line 8, Applicant is respectfully requested to insert a comma between 'benzoyl' and '11C-benzoyl'.

11. It should be noted that the claims have all been examined as if they read on taxanes only.

12. It should be noted that no prior art ahs been found for 11C-paclitaxel and 11C-docetaxel as set forth in dependent claim 3, 7, 12, and 19 wherein the species themselves are directly labeled with carbon-11.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (571) 272-0617. The examiner can normally be reached on Mon.-Fri., 6:45 a.m. - 3:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

D. L. Jones
Primary Examiner
Art Unit 1616

February 19, 2004